

REMARKS

Applicants respectfully request reconsideration of this application, and reconsideration of the Office Action dated September 23, 2003 (Paper No. 16). Upon entry of this Amendment, claims 12, 14, 16, 19, and 23-25 remain pending in this application. Claims 1-11, 13, 15, 17, 18, 20-22 and 26-28 are cancelled and new claims 29-35 are added. The amendments to the claims are supported by the specification and original claims. In addition, newly added claims 29-35 are supported by the specification and original claims. For example, newly added claim 29 is supported by the Sequence Listing and newly added claim 30 is supported at, *inter alia*, page 5, paragraph [0021]. No new matter is incorporated by this Amendment. Furthermore, no additional claim fees are believed due as a result of this Amendment.

Applicants note the Examiner's comments with respect to the Information Disclosure Statements. In response, Applicants file herewith an I.D.S. showing the complete citations of the three references not considered by the Examiner. Since these three references have already been submitted, Applicants respectfully request the Examiner initial next to each reference indicating her consideration of each reference.

With respect to the Examiner's comments on page 15 of the Office Action concerning SEQ ID NO: 1 starting with the "ttg" codon, Applicants make the following remarks. The start codon consists of three nucleotides marking the start of translation. The start codon encodes the first amino acid of the synthesized protein. The methionine encoding codon (ATG) is the universal codon which is used by more than 90% of all genes in the prokaryotes and eukaryotes. For approximately 8% of the genes the start codon comprises GTG, and for a few other genes (including the gene that is the subject matter of the present invention) the start codon comprises TTG. Although the codons GTG and TTG typically encode amino acids that are different from methionine when they are located

inside the protein, all three start codons encode methionine when they are located at the first position of the protein.

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The abstract and Title are objected to. In response, Applicants have amended the Title as suggested by the Examiner. In addition, a new Abstract of the Disclosure incorporating the information suggested by the Examiner is submitted herewith on a separate sheet of paper.

The specification is objected to for purportedly being confusing. The Office Action asserts the phrase “enzyme sigma factor D” is unclear. The Office Action requests clarification. In response, Applicants submit herewith a document which shows that those of ordinary skill would understand the sigD gene to be an RNA polymerase involved in transcription regulation. Hence, the specification as written would not be confusing to those of ordinary skill in the art.

Finally, the specification has been updated to refer to US Pat. No. 6,586, 214 instead of Appln. No. 09/396,478 as suggested by the Examiner.

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Claims 20 and 21 are objected to for purportedly being duplicate claims. Claims 20 and 21 have been cancelled by this Amendment. Hence, the objection is moot.

In addition, claim 25 was objected to for purportedly failing to further limit the claim from which it depends. In response, claim 25 has been amended to recite “*Corynebacterium glutamicum*.” Hence, the objection is overcome and its withdrawal is respectfully requested.

* * *

Claims 12-25 are rejected under 35 U.S.C. § 112, second paragraph, as purportedly indefinite. Applicants note that claims 13, 15, 17, 18, and 20-22 are cancelled. Thus the

rejection as it applied to claims 13, 15, 17, 18, and 20-22 is moot. With respect to the remaining claims, Applicants respectfully traverse this rejection.

The Office Action asserts that the phrase “sigD gene or nucleotide sequences coding for the sigD gene” in claim 12 is indefinite. In response, the claims have been amended to refer to SEQ ID NOs: as suggested by the Examiner.

With respect to claims 23 and 24, these claims have also been amended as suggested by the Examiner.

In view of the above remarks, Applicants respectfully submit that the rejection is overcome. Hence, reconsideration and withdrawal of the rejection are respectfully requested.

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Claims 12-25 are rejected under 35 U.S.C. § 112, first paragraph, as purportedly containing subject matter that is not adequately described by the specification. Applicants respectfully traverse.

The Office Action asserts that the claims are drawn to methods of producing amino acids in coryneform having enhanced a sigD gene, wherein the gene is claimed solely by function.

In response, claim 12 has been amended to recite “A method for the preparation of L-amino acids, comprising culturing coryneform bacteria which include an overexpressed sigD gene having the polynucleotide sequence of SEQ ID NO: 1, in a medium suitable for the expression of the sigD gene to thereby produce L-amino acids.” The specification adequately describes each of the features of amended claim 12. In addition, the specification also describes what is intended by the terminology “overexpressed” and ways to achieve over-expression of the glbO gene. *See pages 10-12.*

Hence, the present claims fully comply with the written description requirements, and withdrawal of the rejection is respectfully requested.

* * *

Claims 12, 14-20, and 22-25 are rejected under 35 U.S.C. § 112, first paragraph, as purportedly containing subject matter that is not fully enabled by the specification. The Office Action asserts that the specification does not enable the full scope of the claimed method. Applicants respectfully traverse.

As stated above, claim 12 has been amended to recite “A method for the preparation of L-amino acids, comprising culturing coryneform bacteria which include an overexpressed sigD gene having the polynucleotide sequence of SEQ ID NO: 1, in a medium suitable for the expression of the sigD gene to thereby produce L-amino acids.” The specification throughout teaches how to make and use the claimed invention. The specification lists numerous examples of Coryneform bacteria which are suitable in the present invention. *See page 6*. The specification also teaches how to achieve overexpression of the glbO gene having SEQ ID NO: 1 and gives examples of types of media useful for producing L-amino acids. *See pages 10-12 and the examples*.

Accordingly, the present claims are fully enabled by the specification, and withdrawal of the rejection is respectfully requested.

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Claim 22 is rejected under 35 U.S.C. § 112, first paragraph, as purportedly not being enabled by the specification. Claim 22 has been cancelled by this Amendment thereby rendering this rejection moot.

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Claim 23 is rejected under 35 U.S.C. § 112, first paragraph, as purportedly not being fully enabled by the specification. The Office Action asserts that the specification does not provide support for “unknown” variations of feedback-resistance aspartase kinase and threonine dehydratase. Applicants respectfully traverse.

Applicants respectfully submit there is no requirement that the specification provide support for “unknown” variations of the claimed subject matter. As stated by the courts, “A specification may, within the meaning of 35 U.S.C. § 112 para. 1, contain a written description of a broadly claimed invention without describing all species that [the] claim encompasses.” *Utter v. Hiraga*, 845 F.2d 993, 998 [6 USPQ2d 1709] (Fed. Cir. 1998). Moreover, “[a]n applicant is not required to describe in the specification every conceivable and possible future embodiment of his invention.” *Rexnord Corp. v. Laitram Corp.*, 274 F.3d 1336, 1344 [60 USPQ2d 1851] (Fed. Cir. 2001). Those of ordinary skill in the art, after reading the present specification, would be able to practice the full scope of claim 23 without undue experimentation. Hence, claims 23 fully complies with 35 U.S.C. § 112. Applicants thus respectfully request that this rejection be reconsidered and withdrawn.

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Claims 12-16, 19-21, and 25 are rejected under 35 U.S.C. § 102(b) as purportedly anticipated by Kimura et al. (EP 0864654). The Office Action asserts Kimura describe every feature of the claimed invention. Applicants respectfully traverse this rejection.

Independent claim 12, from which claims 14, 16, 19, and 25 depend, concerns a method for the preparation of L-amino acids. The method includes culturing coryneform bacteria, which include an overexpressed sigD gene having the polynucleotide sequence of SEQ ID NO: 1, in a medium suitable for the expression of the sigD gene to thereby produce L-amino acids. Kimura neither teaches nor fairly describes a method for preparing amino acids which employ a sigD having the polynucleotide sequence of SEQ ID NO: 1. Hence, Kimura fails to teach or fairly describe each and every feature of the claimed invention and can not anticipate the claims.

Applicants submit that the rejection is overcome and its withdrawal is respectfully requested.

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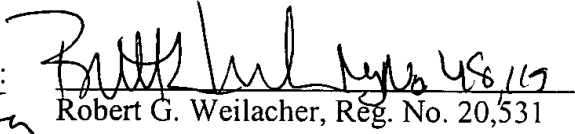
Applicants respectfully submit that this Amendment and the above remarks obviate the outstanding objection and rejections in this case, thereby placing the application in condition for immediate allowance. Allowance of this application is earnestly solicited.

If any fees under 37 C.F.R. §§ 1.16 or 1.17 are due in connection with this filing, please charge the fees to Deposit Account No. 02-4300; Order No. 032301.190.

If an extension of time under 37 C.F.R. § 1.136 is necessary that is not accounted for in the papers filed herewith, such an extension is requested. The extension fee should be charged to Deposit Account No. 02-4300; Order No. 032301.190.

Respectfully submitted,
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RGW/BLN

LISTING OF CLAIMS

Claims 1-11 (cancelled)

Claim 12 (currently amended): A method for the ~~enzymatic production~~ preparation of L-amino acids, comprising

a) ~~fermenting, in a medium,~~ culturing coryneform bacteria ~~producing the desired L-amino acid, in which at least the~~ include an overexpressed sigD gene or nucleotide sequences coding for the sigD gene are enhanced having the polynucleotide sequence of SEQ ID NO: 1, in a medium suitable for the expression of the sigD gene to thereby produce L-amino acids.

Claim 13 (cancelled)

Claim 14 (currently amended): The method according to claim 12, wherein the L-amino ~~acid is~~ acids are lysine.

Claim 15 (cancelled)

Claim 16 (currently amended): The method according to claim ~~15~~ 12, further comprising e) isolating the L-amino acid.

Claims 17 and 18 (cancelled)

Claim 19 (currently amended): The method according to claim 12, wherein the bacteria have been transformed with a plasmid vector ~~that carries the~~ which comprises the nucleotide sequence ~~encoding for the sigD gene~~ of SEQ ID NO: 1.

Claims 20-22 (cancelled)

Claim 23 (currently amended): The method according to claim 12, wherein the bacteria being fermented comprise, at the same time, one or more genes which are ~~enhanced~~ overexpressed; wherein the one or more genes is/are selected from the group consisting of:

- ~~a the gene~~ dapA gene which encodes ~~encoding for~~ dihydrodipicolinate synthase,
- ~~a the gene~~ gap gene which encodes ~~encoding for~~ glyceraldehyde-3-phosphate dehydrogenase,
- ~~a the gene~~ tpi gene which encodes ~~encoding for~~ triosephosphate isomerase,
- ~~a the gene~~ pgk gene which encodes ~~encoding for~~ 3-phosphoglycerate kinase,
- ~~a the gene~~ zwf gene which encodes ~~encoding for~~ glucose-6-phosphate dehydrogenase,
- ~~a the gene~~ pyc gene which encodes ~~encoding for~~ pyruvate carboxylase,
- ~~a the gene~~ mgo gene which encodes ~~encoding for~~ malate-quinone-oxidoreductase,
- ~~a the gene~~ lysC gene which encodes ~~encoding for~~ a feedback-resistant aspartate kinase,
- ~~a the gene~~ lysE gene which encodes a protein ~~encoding for~~ lysine export,
- ~~a the gene~~ hom gene which encodes ~~encoding for~~ homoserine dehydrogenase,
- ~~a the gene~~ ilvA gene which encodes ~~encoding for~~ threonine dehydratase, ~~or the allele~~
- ~~a ilvA(Fbr) gene which encodes ~~encoding for~~ a feedback-resistant threonine dehydratase,~~
- ~~a the gene~~ ilvBN gene which encodes ~~encoding for~~ acetohydroxy acid synthase,
- ~~a the gene~~ ilvD gene which encodes ~~encoding for~~ dihydroxy acid dehydratase, and

~~a the gene zwal gene which encodes coding for the a Zwa1 protein.~~

Claim 24 (currently amended): The method according to claim 12, wherein the bacteria being fermented comprise, at the same time, one or more genes which are ~~attenuated~~ eliminated; wherein the one or more genes is/are selected from the group consisting of:

~~a the gene pck gene which encodes coding for~~ phosphoenol pyruvate carboxykinase,

~~a the gene pgi gene which encodes coding for~~ glucose-6-phosphate isomerase,

~~a the gene poxB gene which encodes coding for~~ pyruvate oxidase,

~~a the gene zwa2 gene which encodes coding for the a Zwa2 protein.~~

Claim 25 (currently amended): The method according to claim 12, wherein ~~microorganisms of the genus the bacteria are~~ Corynebacterium glutamicum ~~are used.~~

Claims 26-28 (cancelled)

Claim 29 (new): The process according to claim 12, wherein said polynucleotide sequence includes nucleotides 301 to 864 of SEQ ID NO: 1.

Claim 30 (new): A process for producing L-amino acids comprising:

a) transforming a Coryneform bacterium with a vector which includes a sigD gene having the polynucleotide sequence of SEQ ID NO: 1, wherein said sigD gene is under the control of a promoter which allows the overexpression of said sigD gene;

b) culturing said bacteria in a medium suitable for expression of the sigD gene to thereby produce L-amino acids; and

c) isolating the L-amino acids.

Claim 31 (new): A method for the preparation of L-amino acids, comprising:

culturing coryneform bacteria, which include an overexpressed sigD gene having a polynucleotide sequence which encodes the amino acid sequence of SEQ ID NO: 2, in a medium suitable for the expression of the sigD to thereby produce L-amino acids.

Claim 32 (new): The method according to claim 31, further comprising isolating the L-amino acids.

Claim 33 (new): The method according to claim 31, wherein the bacteria have been transformed with a plasmid vector which comprises the nucleotide sequence of SEQ ID NO: 1.

Claim 34 (new): The method according to claim 31, wherein the coryneform bacteria produce L-lysine.

Claim 35 (new): A method according to claim 31, wherein the bacteria are *Corynebacterium glutamicum*.

AMENDMENTS TO THE SPECIFICATION

Please replace paragraph [0042] on page 14 of the specification with the following paragraph:

[0042] Furthermore, it may be advantageous for the production of L-amino acids, in addition to the enhancement of the sigD genes also to attenuate, in particular to reduce, the expression of one or more genes selected from the group

- the gene pck coding for phosphoenol pyruvate carboxykinase (DE 199 50 409.1 I.B.R.; DSM 13047),
- the gene pgi coding for glucose-6-phosphate isomerase (US ~~09/396,478~~ Pat. No. 6,586,214 I.B.R.; DSM 12969),
- the gene poxB coding for pyruvate oxidase (DE: 1995 1975.7 I.B.R.; DSM 13114),
- the gene zwa2 coding for the Zwa2 protein (DE: 19959327.2 I.B.R., DSM 13113).

Abstract of the Disclosure

The invention relates to an isolated polynucleotide from *Corynebacterium glutamicum* having a polynucleotide sequence which codes for the sigD gene, and a host-vector system having a coryneform host bacterium in which the sigD gene is present in enhanced form and a vector which carries at least the sigD gene according to SEQ ID No: 1, and the use of polynucleotides which comprise the sequences according to the invention as hybridization probes.